

## REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

Bring completed form for:  
File Information Unit  
Crystal Plaza Three, Room 1001  
2021 South Clark Place  
Arlington, VA  
Telephone: (703) 305-2733

RECEIVED

FEB 09 2004

File Information Unit

In re Application of

Application Number

08-359945

Filed

12-20-94

Paper No.

31

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. \_\_\_\_\_, page \_\_\_\_\_, line \_\_\_\_\_

United States Patent Number 5851832, column \_\_\_\_\_, line \_\_\_\_\_, or

WIPO Pub. No. \_\_\_\_\_, page \_\_\_\_\_, line \_\_\_\_\_

## Related Information about Access to Pending Applications (37 CFR 1.14):

Direct access to pending applications is not available to the public but copies may be available and may be purchased from the Office of Public Records upon payment of the appropriate fee (37 CFR 1.19(b)), as follows:  
For published applications that are still pending, a member of the public may obtain a copy of:

- the file contents;
- the pending application as originally filed; or
- any document in the file of the pending application.

For unpublished applications that are still pending:

- (1) If the benefit of the pending application is claimed under 35 U.S.C. 119(a), 120, 121, or 365 in another application that has: (a) issued as a U.S. patent, or (b) published as a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:

- the file contents;
- the pending application as originally filed; or
- any document in the file of the pending application.

- (2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:

- the pending application as originally filed.

*AC*

Signature

ADEIAN

Typed or printed name

2-9-04

Date

Registration Number, if applicable

7-4861150

Telephone Number

FOR PTO USE ONLY

RECEIVED

Approved by:

FEB 09 2004

Unit:

File Information Unit



US005851832A

**United States Patent** [19]

Weiss et al.

[11] Patent Number: **5,851,832**[45] Date of Patent: **Dec. 22, 1998****[54] IN VITRO GROWTH AND PROLIFERATION OF MULTIPOTENT NEURAL STEM CELLS AND THEIR PROGENY**

[75] Inventors: **Samuel Weiss; Brent Reynolds**, both of Alberta, Canada; **Joseph P. Hammang; E. Edward Bactge**, both of Barrington, R.I.

[73] Assignee: **Neurospheres, Ltd.**, Canada

[21] Appl. No.: **486,648**

[22] Filed: **Jun. 7, 1995**

**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 270,412, Jul. 5, 1994, abandoned, which is a continuation of Ser. No. 726,812, Jul. 8, 1991, abandoned, and a continuation-in-part of Ser. No. 385,404, Feb. 7, 1995, abandoned, which is a continuation of Ser. No. 961,813, Oct. 16, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 359,945, Dec. 20, 1994, abandoned, which is a continuation of Ser. No. 221,655, Apr. 1, 1994, abandoned, which is a continuation of Ser. No. 967,622, Oct. 28, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, and Ser. No. 376,062, Jan. 20, 1995, abandoned, which is a continuation of Ser. No. 10,829, Jan. 29, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 149,508, Nov. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 311,099, Sep. 23, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 338,730, Nov. 14, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812.

[51] Int. Cl.<sup>6</sup> ..... **C12N 5/06; C12N 5/08; C12N 5/02**  
 [52] U.S. Cl. .... **435/368; 435/325; 435/366; 435/383; 435/384**  
 [58] Field of Search ..... **435/240.2, 325, 435/366, 368, 377, 383, 384**

**[56] References Cited****U.S. PATENT DOCUMENTS**

4,753,635	6/1988	Sagen et al.	604/49
4,980,174	12/1990	Sagen et al.	424/563
5,082,670	1/1992	Gage	424/520
5,175,103	12/1992	Lee et al.	435/172.3
5,411,883	5/1995	Boss et al.	435/29
5,612,211	3/1997	Wilson et al.	435/378

**FOREIGN PATENT DOCUMENTS**

0 233 838	8/1987	European Pat. Off.
89/03872	5/1989	WIPO
90/06757	6/1990	WIPO
91/02003	2/1991	WIPO
91/09936	7/1991	WIPO
91/17242	11/1991	WIPO
93/01275	1/1993	WIPO
93/09802	5/1993	WIPO
94/03199	2/1994	WIPO

**OTHER PUBLICATIONS**

Almazan et al., "Epidermal Growth and Bovine Growth Hormone Stimulate Differentiation and Myelination of Brain Cell Aggregates in Culture," *Developmental Brain Research*, 21:257-264 (1985).

Anchan et al., "Trophic Factors Influence Proliferation of Germinal Neuroepithelial Cells of the Retina," *J. Cell Biol.*, 109:58a, Abstract No. 308 (1989).

Anchan et al., "EGF and TGF- $\alpha$  Stimulate Retinal Neuroepithelial Cell Proliferation in Vitro," *Neuron*, 6(6):923-936 (1991).

Bayer et al., "Neuron production in the Hippocampus and olfactory bulb of the adult rat Brain: addition or replacement?," *Annals NY Acad. Sci.* 457:163-172 (1985).

Björklund et al., "Neural Grafting in Animal Models of Neurodegenerative Diseases," *Ann. New York Acad. Sci.*, 457:53-81 (1985).

Bouvier et al., "Basic Fibroblast Growth Factor (bFGF) Promotes the Survival and Proliferation of Mesencephalic Neuronal Precursors in Vitro," *Society for Neuroscience Abstracts*, vol. 18, Abstract No.: 403.7 (1992).

Boyles et al., "Accumulation of Apolipoproteins in the Regenerating and Remyelinating Mammalian Peripheral Nerve," *J. Biol. Chem.*, 265(29):17805-17815 (1990).

Calof et al., "Analysis of Neurogenesis in a Mammalian Neuroepithelium: Proliferation and Differentiation of an Olfactory Neuron Precursor in Vitro," *Neuron*, 3:115-127 (1989).

Cattaneo et al., "Identifying and Manipulating neuronal stem cells," *TINS*, 14(8): 338-340 (1991).

Cattaneo et al., "Proliferation and differentiation of neuronal stem cells regulated by nerve growth factor," *Nature*, 347:762-765 (1990).

Cepko "Immortalization of neural cells via retrovirus-mediated oncogene transduction," *Ann. Rev. Neurosci.*, 12:47-65 (1989).

Deloulme et al., "Establishment of Pure Neuronal Cultures From Fetal Rat Spinal Cord and Proliferation of the Neuronal Precursor Cells in the Presence of Fibroblast Growth Factor," *Journal of Neuroscience Research*, 29:499-509 (1991).

Dunnett et al., "Dopamine-rich transplants in experimental Parkinsonism," *TINS*, 266-270 (Jul. 1983).

Emerich et al., "Behavioral Effects of Neural Transplantation," *Cell Transplantation*, 1:1-27 (1992).

Faaland et al., "Rapid uptake of tyrphostin into A431 human epidermoid cells is followed by delayed inhibition of epidermal growth factor (EGF)-stimulated EGF receptor tyrosine kinase activity," *Mol. Cell Biol.* 11(5):2697-2703 (1991).

(List continued on next page.)

Primary Examiner—George C. Elliott  
 Assistant Examiner—Johnny F. Railey, II  
 Attorney, Agent, or Firm—Flehr Hobbach Test Albritton & Herbert LLP

**[57] ABSTRACT**

A method for the in vitro proliferation and differentiation of neural stem cells and stem cell progeny comprising the steps of (a) isolating the cells from a mammal, (b) exposing the cells to a culture medium containing a growth factor, (c) inducing the cells to proliferate, and (d) inducing the cells to differentiate is provided.

**80 Claims, 3 Drawing Sheets**